REMARKS

Claims 1, 3-7 and 21-27 are pending.

1. Objection to the Specification:

Examiner has objected to the specification due to informalities, namely misspellings and a non-initialed handwritten correction. Applicant is thankful for Examiner's review of the disclosure and has cured such informalities by way of amendments. Applicant has reviewed the specification to correct any other errors and the appropriate corrections have been put in place by way of amendments.

2. Objection to the Claims:

Examiner has also objected to claims 4 and 23, due to the misspelling informality of the word "lupus". Applicant is appreciative of the notice of the informality and has cured the defect by way of amendment.

3. Rejection under 35 U.S.C. § 112, 1st Paragraph:

The pending claims in the present application stand rejected under §112, 1st paragraph. The Examiner finds that the claims contain subject matter not described in the specification to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention. Specifically, Examiner found that while the generalized structure of the fusion protein is well known, it is the identity of the antagonist to be used in the fusion protein which will differ in structure. Further, while T cell receptor antagonists are known for multiple sclerosis, rheumatoid arthritis and Type I diabetes mellitus, the claims as recited to not require any specificity between the antagonist and the associated autoreactive T cells. Based on the arguments submitted below and the claims as presently amended, Applicant respectfully requests Examiner to withdraw the rejection under §112, 1st paragraph.

It is not necessary for the subject matter of the claims to be described literally in the specification. In re Lukach, 169 U.S.P.Q. 795, 796 (C.C.P.A. 1971) Rather, it is sufficient that the specification convey clearly to those skilled in the art that the Applicant invented the specific subject matter later claimed. In re Wertheim, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976)

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 U.S.P.Q. 2d 1961, 1966 (Fed. Cir. 1997) Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Electronics., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 U.S.P.Q. 2d 1641, 1647 (1998); University of California v. Eli Lilly, 119 F.3d 1559, 1566, 43 U.S.P.Q. 2d 1398, 1404 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998).; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 U.S.P.Q. 2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). "Compliance with the written description requirement is essentially a fact-based inquiry that will 'necessarily vary depending on the nature of the invention claimed.'" Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 969-70, 63 U.S.P.Q. 2d 1609, 1617 (Fed. Cir. 2002)

For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. For example, disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a

public depository provides an adequate written description of an antibody claimed by its binding affinity to that antigen. Noelle v. Lederman, 355 F.3d 1343, 1349, 69 U.S.P.Q. 2d 1508, 1514 (Fed. Cir. 2004) (holding there is a lack of written descriptive support for an antibody defined by its binding affinity to an antigen that itself was not adequately described)

Claims 1, 3-7 and 21-27 are directed to use of a fusion protein for treatment of specified autoimmune disorders, namely multiple sclerosis, rheumatoid arthritis and Type I diabetes mellitus. The claim language details, with sufficient clarity, the precise mechanism utilized by said fusion protein. Applicant respectfully submits that the claims, as presently recited, require that the T cell antagonist be specific for autoreactive T cells associated with said autoimmune disorders. Specifically, the claims now recite the limitation of the T cell receptor antagonist being specific for the autoreactive T cells associated with the autoimmune disease.

Additionally, Examiner has raised an issue with the type of diabetes referred to in the claims. Applicant agrees with Examiner that some Type II diabetic patients are insulin dependent. Thus, because Type II diabetes is not considered an autoimmune disease, Applicant has amended all relevant claims to the autoimmune disease which would be treated by Applicant's fusion protein, namely Type I diabetes mellitus.

Therefore, Applicant respectfully requests Examiner withdraw the previous rejection with respect to claims 1, 3-7 and 21-27 under §112, 1st paragraph, in light of the above offered arguments and amendments to the claims.

4. Rejection under 35 U.S.C. § 102

Examiner has rejected claims 1, 3-4 and 21-24 under § 102(e) as being anticipated by US Patent No. 5,837,243 ("Deo"). Examiner is of the opinion that the structure of the fusion protein taught by Deo meets all of the claimed limitations as Applicant's invention. Based on the following arguments, as well as the claims pr esented as

currently amended, Applicant respectfully traverses the rejection as the claims are now patentably distinguishable over the Deo reference.

In order for a reference to qualify as prior art under 35 U.S.C. § 102, the reference must "anticipate" the claimed invention. More specifically, the reference must disclose each and every element of the claimed invention (MPEP § 2131; Verdegaal Bros. v. Union Oil Co. of Cal., 814 F.2d 628, 631 (Fed. Cir. 1987); Scripps Clinic & Res. Found. v. Genentech, Inc., 927 F.2d 1565, 1576 (Fed. Cir. 1991); In re Schreiber, 128 F.3d 1473, 1477 (Fed. Cir. 1997); Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047 (Fed. Cir. 1995). The absence of any claimed element in the prior art reference negates anticipation.

Anticipation analysis under § 102 is a two-step process. First, all elements of the claims must be properly construed (Elmer v. ICC Fabricating, Inc., 67 F.3d 1571, 1574 (Fed. Cir. 1995). Second, it must be determined whether all elements of the claims, as properly construed, are disclosed in the prior art reference, either explicitly or implicitly (See Schreiber at 1477; Glaxo at 1047).

The first step in the analysis involves properly construing all elements of the claims at issue. The present invention claims a fusion protein to alleviate specific autoimmune disorders, comprising an Ig molecule linked to one or more T cell receptor antagonists. Further, the claims as currently drafted include the specific mechanism of action of said fusion protein and will be construed as having the capability of:

i) binding to an Fc receptor of an antigen presenting cell (APC);
ii) being endocytosed by said APC;
iii) binding to newly synthesized MHC Class II molecules once inside said APC;
iv) forming a complex with said MHC molecules which migrates to the cell surface of said APC;
v) engaging autoreactive T cells, thereby reducing cytokine production and ultimately inactivating the autoreactive T cells specific for the T cell antagonist.

(See Claim 1). Applicant respectfully proffers the above as properly construing all elements of Claim 1, where such an interpretation includes all the limitations set forth in the recent amendments to the claims in the present Office Action response. Support for the recent amendments is found throughout the specification (for just a partial list of support in the disclosure, please see Page 3, Lines 14-18; Page 6, Lines 28-30; Page 11, Lines 23-30; Page 12, Lines 1-12, 27-30; Page 13, Lines 1-11)

Now that all elements of the claims have been properly construed, the second step in an anticipation analysis examines whether all elements of the claims, as properly construed, are disclosed in the prior art reference. Applicant's invention is directed to a fusion protein endowed with, and limited to, the descriptions previously mentioned. Deo, on the other hand, operates via a different mechanism, namely one competitive in nature. Specifically, from Example 7, Deo teaches use of a construct in a competitive mechanism by the T cell antagonist operating by occupying either the MHC Class II molecules, T cell receptor binding or both, resulting in an inhibition of T cell activation. Applicant's invention works by subjecting the fusion protein to an endocytotic event by the APCs and, once internalized, forming complexes with newly synthesized MHC Class II molecules which will engage the autoreactive T cells, eventually reducing cytokine production and inactivating the autoreactive T cells. Because Deo function through a competitive mechanism, it is unlikely that the fusion construct taught by Deo would be sufficient to overcome the continuous synthesis of MHC molecules and pathogenic peptides. Applicant's invention, on the other hand, is implicated in the process at an earlier stage. The fusion protein is able to form complexes with newly synthesized MHC molecules when endocytosed by the APCs, and the interaction of the antagonist/MHC complexes with the autoreactive T cells lead to inactivation of the autoreactive T cells. This is in stark contrast to binding the MHC at a later stage, as in Deo, where the competition between MHC binding and TCR binding will result in the disablement of the fusion protein due to the flow of the continuous synthesis of MHC molecules and pathogenic peptides. Because the Deo reference fails to teach all elements of Applicant's claims, as the claims now recite the limitations of the mechanism of action of Applicant's

fusion protein after internalization by the APCs, the second step in the anticipation analysis has failed, resulting in Applicant's invention not being anticipated by Deo, rendering the § 102 rejection improper.

Applicant understands that arguments directed toward unclaimed features of the invention are both unpersuasive and irrelevant. Because claims 1, 3-4 and 21-24 as currently presented reflect the above mentioned limitations, Applicant respectfully traverses the § 102 rejection. As Deo does not anticipate Applicant's invention as claimed, rendering the rejection as improper. Applicant respectfully requests Examiner withdraw the rejection in light of the arguments above and the claims as currently amended.

5. Rejection under 35 U.S.C. § 103: Deo et al in view of Karin et al

The Examiner has rejected claims 1, 5, 21 and 25 under § 103 as being unpatentable over Deo et al in view of Karin et al. Examiner is of the opinion that one of ordinary skill in the art would have been motivated to combine the T cell antagonist peptide derived from myelin basic protein of Karin and insert it into the fusion construct of Deo, thereby arriving at Applicant's claimed invention. Even assuming this combination of Deo and Karin, Applicant respectfully submits there would still remain the mechanistic distinctions between the Deo fusion construct and Applicant's fusion protein, as previously described.

Applicant respectfully submits that an analysis of the application of 35 U.S.C. § 103 is not appropriate in this instance, as the references cited by Examiner are not combinable because the resulting combination is not the claimed invention. Patentability has not been determined on the basis of the obviousness of structure alone. In re Papesch, 50 C.C.P.A. 1084; 315 F.2d 381 (1963). Further, Courts determine the unobviousness and patentability of new chemical compounds by taking into consideration their biological or pharmacological properties. Id. Similarly, if a protein shows a different interaction than another protein, there may be an assumption of a difference in

structure between the proteins. In other words, though we cannot say for certain what the structural differences are, they must exist; otherwise the proteins would exhibit the same interactions.

The Deo fusion construct, with Karin's TCR antagonist peptide, would be mechanistically distinct from Applicant's invention, as the fusion protein of the present application *prevents* activation of autoreactive T cell well upstream of Deo's invention, which is limited to *inhibiting* T cell activation after the MHC molecules and pathogenic peptides are synthesized. Thus, the Deo invention enters the arena at too late a stage to have much of a beneficial impact, whereas Applicant's fusion protein inactivates autoreactive T cells by way of the interaction between the antagonist/MHC complexes and the autoreactive T cells.

As the limitations described above are recited in the claims and based on the above mentioned arguments, Applicant respectfully requests Examiner withdraw the § 103 rejection relative to Deo et al in view of Karin et al for independent claims 1 and 21. As the dependent claims are nonobvious under § 103 if the independent claims from which they depend are nonobvious, Applicant respectfully requests Examiner withdraw the rejection relative to the dependent claims 5 and 25 as well. (Hartness Int'l, Inc. v. Simplimatic Eng'g Co., 819 F.2d 1100, 1108, 2 USPQ2d 1826, 1831 (Fed. Cir. 1987); In re Abele, 684 F.2d 902, 910, 214 USPQ 682, 689 (CCPA 1982); In re Semaker, 702 F.2d 989, 991, 217 USPQ 1, 3 (Fed. Cir. 1983).

7. Rejection under 35 U.S.C. § 103: Deo et al in view of Kuchroo et al

The Examiner has rejected claims 1, 6, 21 and 26 under § 103 as being unpatentable over Deo et al in view of Kuchroo et al. Examiner is of the opinion that one of ordinary skill in the art would have been motivated to combine the T cell antagonist peptide derived from myelin proteolipid protein of Kuchroo and insert it into the fusion construct of Deo, thereby arriving at Applicant's claimed invention. Even assuming this combination of Deo and Kuchroo, Applicant respectfully submits there would still remain

the mechanistic distinctions between the Deo fusion construct and Applicant's fusion protein, as previously described. The Deo fusion construct, with Kuchroo's TCR antagonist peptide, would be mechanistically distinct from Applicant's invention, as the fusion protein of the present application *prevents* activation of autoreactive T cell well upstream of Deo's invention, which is limited to *inhibiting* T cell activation after the MHC molecules and pathogenic peptides are synthesized. Thus, the Deo invention enters the arena at too late a stage to have much of a beneficial impact, whereas Applicant's fusion protein inactivates autoreactive T cells by way of the interaction between the antagonist/MHC complexes and the autoreactive T cells.

Applicant respectfully submits that based on the mechanistic distinctions between the claimed invention and the Deo reference, the § 103 rejection is overcome, regardless of which peptide is inserted into Deo's fusion construct. The fact that Deo operates in a different manner precludes a § 103 rejection, whether based solely on Deo et al or in conjunction with another reference citing a peptide for insertion into Deo's fusion construct. Therefore, Applicant respectfully requests Examiner to withdraw the § 103 rejection based on the above mentioned arguments and the claims are presently presented.

8. Rejection under 35 U.S.C. § 103: Deo et al in view of Elliot et al, Kuchroo et al and Karin et al

The Examiner has rejected claims 1, 7, 21 and 27 under § 103 as being unpatentable over Deo et al in view of Elliot et al, Kuchroo et al and Karin et al. As discussed supra, regardless of whether you insert one peptide into Deo's fusion construct or, as Elliot suggests, multiple epitopes, one is still left with the distinction previously discussed between the claimed invention and the fusion construct described by Deo. As combining Deo with either Elliot, Kuchroo, Karin or all three still falls short of treating autoimmune diseases by preventing activation of autoreactive T cells in the manner recited in the claimed invention, Applicant respectfully requests Examiner withdraw the §

103 rejection as it relates to Deo in view of Elliot, Kuchroo and Karin based on the above mentioned arguments and the claims as presently presented.

9. Double Patenting Rejection:

Claims 1, 3-4, 6, 21-24 and 26 stand rejected under obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,737,057 ('057). Examiner finds that the claims of the present invention are not patentably distinct from the '057 patent.

Applicant respectfully submits that based on the claims as currently presented, Examiner should withdraw the double patenting rejection, as the rejection is cured by way of amendments. Specifically, the '057 claims a composition comprising an Ig molecule linked to a T cell antagonist to eventually affect autoreactive T cell in vivo. The present invention, on the other hand, is much more specific in terms of the action of the fusion protein. Firstly, the claims in the present application refer to use of the fusion protein to treat specified autoimmune disorders. The claims of the '057 application do not specify which autoimmune disorders would be affected by the '057 composition. Secondly, the claims as presented in the present application have been amended to include language detailing the requisite specificity of the T cell antagonist to be used. The T cell receptor antagonist(s) will be specific for autoreactive T cells associated with the autoimmune disease to be treated. Thus, there is a deeper level of specificity in the present application relative to the '057 application, which requires no specificity for either the T cell receptor antagonist itself or the autoimmune disease to be treated.

Applicant respectfully requests Examiner withdraw the double patenting rejection in light of the present amendments to the claims which change the scope of said claims such that they are no longer anticipated by the '057 claims.

10. New § 112 Rejection: Janeway et al

Examiner has raised a new § 112 rejection based on Applicant's amendments to the claims of March 21, 2005. Applicant respectfully requests Examiner withdraw this new § 112 rejection based on the claims as currently presented for the reasons put forth below.

Janeway et al teaches that because different autoantigens are recognized in different autoimmune diseases, it is not likely that an antagonist associated with one particular disease would be useful in treating another disease due to the lack of specificity. As such, Examiner believes that the antagonists used in the claimed fusion protein must be specific for the disorder being treated. Applicant agrees with the Examiner on this point and has cured such defect by way of amendment. The claims, as currently recited, now contain language which goes to the requisite specificity of the fusion protein and, more specifically, for the T cell antagonist to be used. As such, Applicant respectfully requests withdrawal of the § 112 rejection, as the defect is cured by way of amendment.

Applicant respectfully requests withdrawal of the above identified rejections and allowance of the present application based on Applicant's arguments and amendments. Applicant is applying for a two month extension of time and a Request for Continued Examination. If there are any questions or comments, Applicant's attorney may be reached at the telephone number state below.

Respectfully submitted,

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